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(54) Title: TREATMENT OF HERPETIC DISEASES (57) Abstract A method of prophylactic or therapeutic treatment of a human or animal body comprising by application of a pharmaceutically acceptable amount by oral, parenteral or topical application of zinc glycerolate for the treatment of herpetic diseases other than Herpes Simplex. The herpetic diseases may be Herpes Zoster or Genital Herpes. The application of zinc glycerolate may be as a dry powder, as a cream or ointment or applied topically by an applicator.		

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TREATMENT OF HERPETIC DISEASES

INTRODUCTION

This invention relates to a zinc glycerol complex when used for the treatment of herpetic diseases of the human or animal body .

5 BACKGROUND OF THE INVENTION

The preparation of compounds of glycerol with the transition metals has been described in "*Crystalline cobalt, zinc, manganese and iron alkoxides of glycerol*" by E. W. Radoslovich, M. Raupach, P. G. Slade and R. M. Taylor in Australian Journal of Chemistry 23, 1963 - 1970, (1970). These compounds form during
10 the heating of particular metal oxides, hydroxides or salts with glycerol at temperatures around 120° C or higher. In particular the compound with zinc is of interest. The compound of zinc with glycerol is Zinc (1,2,3 - Propanetriolato [2-] - O₁, O₂) homopolymer, stereoisomer and may be termed zinc monoglycerolate, glycerato zinc, zinc glycerolate and colloquially "glyzinc".

15 The term zinc glycerolate will be used in this specification.

The compound is described for instance in P.C.T. International Publication WO82/01867 in the names of Taylor and Brock, and comprises a specific product of a reaction between certain zinc compounds and glycerol at certain temperature ranges. The compound is described as having uses in the
20 therapeutic or prophylactic treatment of disorders of the human or animal skin. It is suggested that the compound may have cosmetic uses and is suggested for the compounding of shaving cream and as a topical application for the prevention of sunburn.

In WO82/01867 zinc glycerolate is mentioned as having a number of
25 prophylactic and therapeutic uses. Thus it is mentioned as being effective in the treatment and prevention of ammoniacal dermatitis (burns in the genital area of babies which originate from ammonia liberated during the decomposition of urine - nappy rash), in the treatment of pruritus, especially in people confined to bed or immobility, for the alleviation of psoriasis, for the treatment and
30 prevention of fungal or bacteriological decomposition of tissue and the resultant odours arising in such complaints as tinea pedis and for the prevention of industrial dermatitis arising from particular environments.

Reference is also made to P.C.T. International Application WO87/01281 in the name of the present applicant, which unlike the first referred to P.C.T.

application refers to the use of the zinc glycerolate as a per oral treatment for gastric bleeding or ulceration or in a topical application as a depot for the slow release of the compound and refers to diffusion through the skin for the treatment of arthritis and zinc insufficiency and includes psoriasis, and refers
5 also to tests against various organisms including fungi, but does not suggest effects in the diseases set out in this specification nor does it suggest prophylactic treatments which it has now been found to have.

In a publication of the Medical Journal of Australia Volume 152 January 1 st 1990 at page 54 clinical trials in Thailand are described which show the use of
10 Zinc Glycerolate was found to be effective against oral Herpes Simplex sores caused by the virus *Herpes Simplex I*. Although this is a disclosure of the use of the compound for a specific herpetic disease in no other case has a topical application for Herpes Simplex been found to be a therapy for other varieties of herpetic infections. Therefore response to a condition or disease induced by a
15 different virus to this earlier therapy could be viewed certainly as an unexpected step.

Hence the results in the present invention are as quite unexpected as were the first referred to in the publication of Taylor and Brock which does not include reference to these diseases or conditions for which it has now found to be
20 useful but was directed to mainly skin ailments such as sunburn and it is surprising that it can provide a therapy for a virally induced disease or condition such as those now found and described.

BRIEF DESCRIPTION OF THE INVENTION

In one form therefore the invention is said to reside in a method of treatment of
25 a human or animal body comprising the step of application of a pharmaceutically acceptable amount by oral, parenteral or topical application of zinc glycerolate for the treatment of the herpetic disease Herpes Zoster in prophylactic or therapeutic treatment.

Herpes Zoster or shingles is caused by the virus *Varicella zoster*. This virus
30 can also cause Chicken Pox and the application of the compound of the present invention may also be useful for the prevention of that disease.

Another herpetic diseases to which the present invention is applicable is Genital herpes caused by the virus *Herpes simplex II*.

In another form the invention may be said to reside in a method of treatment of a human or animal body comprising the step of application of a pharmaceutically acceptable amount by oral, parenteral or topical application of zinc glycerolate for the treatment of the herpetic disease Genital Herpes in
5 prophylactic or therapeutic treatment.

In a further form the invention is said to reside in the use of zinc glycerolate in a pharmaceutically acceptable amount by oral, parenteral or topical application for the prophylactic or therapeutic treatment of the herpetic diseases Herpes Zoster and Genital herpes.

10 In a still further form the invention can be said to reside in zinc glycerolate when used as a pharmaceutical in a pharmaceutically acceptable amount by oral, parenteral or topical application the treatment of the herpetic diseases Herpes Zoster and Genital herpes for prophylactic or therapeutic treatment.

The unsuspected and surprising discovery is that the use of zinc glycerolate as
15 an anti-viral drug appears to provide relief from the symptoms of these diseases and also appears to provide some alleviation of the underlying causes of these diseases.

Application of zinc glycerolate can be topical and can be applied as a dry powder or as a suspension in a suitable liquid medium or semisolid medium
20 such as a cream or ointment and can be applied topically by an applicator (e.g. by transdermal delivery patch) where internal mobilisation in the blood is required for transport to other internal remote areas. Alternatively it can be applied by parenteral means such as by injection in a suitable suspension or solution. Oral intake in the form of a tablet, capsule or lozenge may also be
25 suitable for some applications of the invention.

One suitable way of treatment might include application as a cream or ointment including in its formulation zinc glycerolate to the affected body part.

It is believed that the action of zinc glycerolate for treatment in the ways as discussed above relates to the ability of the compound to be easily adsorbed
30 into the human or animal body and to release the zinc from within the compound in a form that is readily useable.

Hence unexpectedly it appears that the application of the zinc glycerolate has a beneficial effect in alleviating the symptoms of or treating a number of diseases that are not caused by infection or mechanical injury.

The applicant's have carried out tests to determine the effectiveness of the zinc glycerolate from the conditions and diseases enumerated herein and believe that the results achieved in showing the effectiveness of a compound for treatment of these are entirely unsuspected.

5 DESCRIPTION OF THE PREFERRED METHOD AND EXAMPLE

Herpes Zoster

Patients were examined with treatment using zinc glycerolate in the form of a powder plus other treatments. Examination of patients was carried out every three days.

- 10 Five patients with Herpes Zoster were investigated. Immunostimulation, analgesic and vitamin treatments were administered additionally. Local zinc glycerolate treatment showed an anti-inflammatory effect. Regression of vesicles and infiltration were observed. In all five cases local status of patients was much or very much improved.

- 15 Details of the treatment of the five patients were as follows:

- 1 Treatment with Vitamin B1 and zinc glycerolate. Decrease in erythema and some itching was seen. Rapid crusting of the lesions. Patient was very satisfied with treatment.
- 20 2 Treatment with Isoprinosine, Vitamin B1, Pyralgin, Reladom, and zinc glycerolate. No change in pain and loss of sleep. Crusting of lesions within three days. Patient was satisfied with treatment.
- 3 Treatment with zinc glycerolate . No previous treatment. Less Pain. Crusting within three days. Satisfactory improvement within six days.
- 4 Treatment with Isoprinosine and zinc glycerolate. No previous treatment.
25 Decrease in pain, burning and itching. Very rapid effect of treatment.
- 5 Treatment with Vitamin B1, Pyralgin, and zinc glycerolate. Erythema decreased. No change in pain or itching initially. Rapid crusting of lesions. Completed treatment in thirteen days.

Isoprinosine, antiviral, made by Newport Pharma USA

- 30 Pyralgin, analgesic; Relanorm, anxiolytic, made by Polfa, Poland.

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Claims :

1. A method of treatment of a human or animal body comprising the step of application of a pharmaceutically acceptable amount by oral, parenteral or topical application of zinc glycerolate for the treatment of herpetic diseases other than Herpes Simplex for prophylactic or therapeutic treatment.
- 5 2. A method of treatment as in Claim 1 wherein the herpetic disease is Herpes Zoster or shingles
3. A method of treatment as in Claim 1 wherein the herpetic disease is Genital herpes.
4. A method of treatment as in Claim 1 wherein the application of zinc
10 glycerolate is selected from the group of topical application, for instance as a dry powder, by suspension in a suitable liquid or semi-solid medium, for instance as a cream or ointment or applied topically by an applicator.
5. A method of treatment as in Claim 1 wherein the application of zinc
15 glycerolate is parenteral means such as by injection in a suitable suspension or solution.
6. A method of treatment as in Claim 1 wherein the application of zinc glycerolate is in the form of a tablet, capsule or lozenge.
7. The use of zinc glycerolate in a pharmaceutically acceptable amount by
20 oral, parenteral or topical application for the prophylactic or therapeutic treatment of herpetic diseases other than Herpes Simplex.
8. Zinc glycerolate when used as a pharmaceutical for prophylactic or therapeutic treatment in a pharmaceutically acceptable amount by oral, parenteral or topical application the treatment of herpetic diseases other than Herpes Simplex.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU 93/00353

A. CLASSIFICATION OF SUBJECT MATTER Int. Cl. ⁵ A61K 31/315 According to International Patent Classification (IPC) or to both national classification and IPC				
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC : A61K 31/315 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched AU : IPC as above Electronic data base consulted during the international search (name of data base, and where practicable, search terms used) WPAT JAPIO				
C. DOCUMENTS CONSIDERED TO BE RELEVANT				
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to Claim No.		
X	AU,A, 62865/86 (GLYZINC PHARMACEUTICALS LIMITED) 12 March 1987 (12.03.87) whole document	1-8		
X	WO,A, 82/01867 (TAYLOR, Reginald Morton et al) 10 June 1982 (10.06.82) whole document	1-8		
<div style="display: flex; justify-content: space-between; align-items: center;"> <div style="text-align: center;"> <input type="checkbox"/> Further documents are listed in the continuation of Box C. </div> <div style="text-align: center;"> <input checked="" type="checkbox"/> See patent family annex. </div> </div>				
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; vertical-align: top;"> <p>* Special categories of cited documents :</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </td> <td style="width: 50%; vertical-align: top;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</p> <p>"&" document member of the same patent family</p> </td> </tr> </table>			<p>* Special categories of cited documents :</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p>	<p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</p> <p>"&" document member of the same patent family</p>
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Date of the actual completion of the international search 29 October 1993 (29.10.93)		Date of mailing of the international search report 5 NOV 1993 (5.11.93)		
Name and mailing address of the ISA/AU AUSTRALIAN INDUSTRIAL PROPERTY ORGANISATION PO BOX 200 WODEN ACT 2606 AUSTRALIA Facsimile No. 06 2853929		Authorized officer  J.P. PULVIRENTI Telephone No. (06) 2832261		

Information on patent family members

PCT/ 93/00353

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report				Patent Family Member			
AU	62865/86	GB	2191941	JP	63500664	WO	87/01281
WO	82/01867	AU	78032/81	DE	3152555	FR	2494583
		GB	2101132	JP	57501783	JP	2056337
		US	4544761				